RINGKASAN

EFEKTIVITAS DAN STABILITAS FISIKOKIMIA NANOSTRUCTURED LIPID CARRIER COENZYME Q10 PADA BERBAGAI RASIO LIPID SETIL PALMITAT DAN ALFA TOKOFERIL ASETAT SEBAGAI PEMBAWA

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Nanoteknologi merupakan manipulasi materi pada skala atomik dan skala molekular. Kombinasi dari beberapa atom membentuk molekul dengan kisaran ukuran pada skala nano yaitu sekitar 0,2-1000 nm. Nanopartikel alternatif yaitu NLC (*Nanostructured Lipid Carrier*) sebagai generasi terbaru banyak diteliti dalam beberapa tahun terakhir karena memiliki berbagai kelebihan

NLC terdiri dari matriks lipid padat dan lipid cair dalam jumlah tertentu. NLC yang terdiri atas campuran lipid padat dan lipid cair mampu mengakomodasi ruang yang dibutuhkan untuk penjebakan bahan obat. NLC tetap dalam bentukan padatnya dengan cara mengendalikan kadar lipid cair yang ditambahkan ke dalam formulasi, sehingga sifat pelepasan obat terkontrol untuk NLC dapat dicapai. Salah satu bidang bahan yang membutuhkan aplikasi sistem penghantaran obat dengan pelepasan terkendali dan menjamin stabilitasnya adalah antioksidan.

Coenzyme Q10 berbentuk serbuk kristalin, tidak larut dalam air, memiliki sifat lipofilisitas yang tinggi. Kelarutan Coenzyme Q10 di air sangat rendah (4 ng/ml), menyebabkan bioavailabilitas dan permeabilitas rute pemakaian oral yang rendah. Senyawa antioksidan merupakan senyawa yang tidak stabil dengan adanya cahaya dan bahan-bahan pengoksidasi yang ada di udara. Salah satu isu utama dari penggunaan Coenzyme Q10 ini terkait dengan efikasi potensial yang ditentukan oleh absorbsi dan bioavailabilitas. Coenzyme Q10 memiliki struktur kimia yang kompleks sehingga formulasi yang dilakukan harus mendapatkan produk dengan stabilitas baik dan efektif.

Untuk mendapatkan campuran terbaik dari matriks partikel NLC, maka lipid padat dicampur dengan lipid cair, dalam rasio 70:30 sampai dengan rasio 99,9: 0,1.

Efektifitas dari sistem NLC ditentukan oleh efisiensi penjebakan. Efisiensi penjebakan sendiri dipengaruhi oleh perbandingan jumlah lipid padat dan lipid cair yang digunakan serta ukuran partikel dari sistem. NLC yang terbentuk dalam sistem dapat meningkatkan drug loading karena peningkatan jumlah lipid cair pada suatu formula dapat meningkatkan efisiensi penjebakannya. Dimana penjebakan bahan aktif tersebut juga dapat berpengaruh pada proses lepasnya bahan aktif dari sistem. Sedangkan lipid padat sebagai matriks padat pada sistem NLC berperan dalam melindungi bahan aktif dari degradasi kimia dan memberikan fleksibilitas yang tinggi dalam mengatur pelepasan bahan aktif. Dalam suatu sistem NLC dapat ditambahkan surfaktan atau emulsifier. Surfaktan ditambahkan untuk menstabilkan nanopartikel yang terbentuk pada sistem serta mencegah adanya penggabungan partikel selama penyimpanan.

Pada penelitian ini, dilakukan dua tahap utama yaitu optimasi perbandingan lipid cair alfa tokoferil asetat dan lipid padat setil palmitat dengan jumlah surfaktan Tween 80 dan kosurfaktan propilenglikol yang tetap. Optimasi perbandingan komposisi lipid padat dan lipid cair sistem NLC Coenzyme Q10 dilakukan pada tiga perbandingan yaitu 70:30; 80:20; dan 90:10. Formula dengan perbandingan 70:30 menunjukkan pelepasan in vitro yang lebih tinggi, memiliki karakteristik yang diharapkan dan penetrasi in vivo yang paling tinggi dibandingkan dua formula yang lain. Oleh karena itu, sistem NLC Coenzyme Q10 formula 70:30 dipilih untuk dilanjutak uji stabilitas selama 90 hari. Hasil uji stabilitas menunjukkan bahwa sistem NLC Coenzyme Q10 dengan perbandingan 70:30 stabil selama penyimpanan.

SUMMARY

EFFECTIVENESS AND PHYSICOCHEMICAL STABILITY OF NANOSTRUCTURED LIPID CARRIER COENZYME Q10 IN DIFFERENT RATIO of LIPID ALFA CETYL PALMITATE AND TOCOPHERYL ACETATE AS CARRIER

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Nanotechnology is a manipulation of substance at the nanoscale which is about 0.2 to 100 nm. NLC alternate carrier (Nanostructured Lipid Nanoparticles) as the latest generation widely studied in recent years because it has many advantages.

NLC (Nanostructured Lipid Carrier) consists of a matrix of solid lipid and liquid lipid in a certain amount. NLC which consists of a mixture of solid lipid and liquid lipid is able to accommodate the space needed for entrapping drug substance. NLC remains in the formation of the solid by controlling the levels of lipid liquid were added to the formulation, so that controlled drug release properties for the NLC can be achieved. One area of materials that require the application of drug delivery systems with controlled release and ensures stability is antioxidant.

Coenzyme Q10 shaped crystalline powder, insoluble in water, has a high lipophilicity properties. Coenzyme Q10 solubility in water is very low (4 ng / ml), causing low bioavailability and permeability of the oral administration. Antioxidant compounds are compounds that are not stable in the presence of light and oxidizing substances present in the air. One of the main issues of the use of Coenzyme Q10 is related to the potential efficacy as determined by absorption and bioavailability. Coenzyme Q10 has a complex chemical structure that formulations do have to get a product with good stability and effective.

In order to get the best mix of NLC particle matrix, the solid lipid is mixed with a liquid lipid, in a ratio of 70:30 to a ratio of 99.9: 0.1. The effectiveness of the system is determined by the NLC trapping efficiency. The efficiency of trapping itself affected by the ratio of the amount of solid lipid and liquid lipid used and the particle size of the system. NLC formed in the system can increase drug loading because of the increased amount of lipid liquid on a formula can improve the

efficiency penjebakannya. Where is the entrapping the active ingredient can also influence the process of release of the active ingredients of the system. While the solid lipid matrix NLC solid system play a role in protecting the active ingredient from chemical degradation and provide greater flexibility in arranging the release of the active ingredient. NLC in a system can be added surfactants or emulsifiers. Surfactants are added to stabilize the nanoparticles formed in the system and prevent their incorporation of particles during storage.

In this study, carried out two main stages, namely the optimization of lipid ratio of alpha tocopheryl acetate as liquid lipid and cetyl palmitate as solid lipid by the number of fixed Tween 80 as surfactant and propyleneglycol as cosurfactant. Optimization of lipid composition ratio of solid and liquid lipid NLC Coenzyme Q10 system performed on three comparisons is 70:30; 80:20; and 90:10. Formula with a ratio of 70:30 shows the in vitro release were higher, had the expected characteristics and in vivo penetration of the highest compared to the other two formulas. Therefore, the NLC system Coenzyme Q10 formula 70:30 selected for stability testing for 90 days. The test results show that the stability of the system NLC Coenzyme Q10 with a 70:30 ratio was stable during storage.

ABSTRACT

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The aim of this study was to investigate physical characteristics of NLC mixture of alpha tocopheryl acetate, cetyl palmitate, Tween 80 and propyleneglycol using High Shear Homogenization technique on NLC preparation to predict the optimum ratio of alpha tocopheryl acetate-cetyl palmitate to produce good characteristics of NLC loaded Coenzyme, higher %EE, good penetration, controlled release and stable.

Lipid characterizations were conducted by Diffraction Scanning Calorimetry (DSC), X-Ray Diffraction (XRD) and FTIR Spectrophotometri. Coenzyme Q10 concentration was measured by spectrophotometer at 275 nm. NLC characteristics based on their morphology was determined using Transmission Electron Microscope (TEM), particle size and its polidispersity index which were measured with Delsa Nano™ Particle Size Analyser (PSA). Percentage of Coenzyme Q10 entrapped in NLC was determined by dialysis bag method. Coenzyme Q10 release profile were measured using with Franz cell for 12 hours. Penetration depth of NLC Coenzyme Q10 in abdominal skin of Wistar rat was determined with fluorescence microscopy using rhodamine B as marker. NLC physical stability based on minimum of particle size variation, pH and visscosity during 90 days storage.

The result showed that formula with ratio of cetyl palmitate-alpha tocopheryl acetate 70:30 (% w/w) produce good characteristics of NLC loaded Coenzyme, higher %EE, good penetration, controlled release and stablein 90 days storage.

Keywords: Coenzyme Q10, Nanostructured Lipid Carrier (NLC), cetyl palmitate, alpha tocopheryl acetate, high shear homogenization